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(71) Applicant *(for all designated States except US)*: UNI–CI S.R.L. [IT/IT]; Via Zuretti, 2, I–20125 Milano (IT).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: DALL'AGLIO, Roberto [IT/IT]; Via Montanara, 102, I–43100 Parma (IT). BORGONOVO, Margherita [IT/IT]; Via Francesco Melzi D'Eril, 7, I–20154 Milano (IT). INTROINI, Carlo [IT/IT]; Piazza Firenze, 19, I–20149 Milano (IT). MELEGARI, Pierangelo [IT/IT]; Via Fochi, 3, I–43027 San Prospero (IT).

(74) Agents: MANCINI, Vincenzo et al.; Ing. A. Giambrocono & C. s.r.l., Via Rosolino Pilo, 19/b, I–20129 Milan (IT).

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(54) Title: PHARMACEUTIC, DIETETIC AND COSMETIC COMPOSITIONS BASED ON THIOCTIC ACID AND CYSTEINE

(57) Abstract

Novel pharmaceutic, dietetic and cosmetic compositions, based on tioctic acid and cysteine and/or a pharmaceutically, dietetically or cosmetically acceptable derivative thereof, useful for the prevention and treatment of conditions caused by oxidative stresses and alterations of both aerobic and anaerobic energetic metabolism by activation of mitochondrial energetic enzyme systems (glycolysis and lipolysis) are described.

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PHARMACEUTIC, DIETETIC AND COSMETIC COMPOSITIONS BASED ON THIOCTIC ACID AND CYSTEINE

* * * * * * *

The present invention concerns, novel pharmaceutic, dietetic and cosmetic compositions useful for the prevention and treatment of conditions caused by oxidative stresses and alterations of mitochondrial energetic metabolism.

The compositions of the invention comprise in particular tioctic acid and cysteine and/or a pharmaceutically, dietetically or cosmetically acceptable derivative thereof.

Tioctic acid, known also as α-lipoic acid, is employed in the treatment of hepatic pathologies and as an antidote for poisonous mushrooms of Amanita species genus.

It is known that tioctic acid, owing to its structure, is both watersoluble and liposoluble in nature and has therefore the capability of acting equally in intracellular and extracellular environment and reducing both the endogenous and exogenous free-radicals.

Cysteine is a semi-essential amino acid, component of glutathione, cystine and many other proteins; it is stable in acid environment and is employed as a detoxicating agent.

It is further known that cysteine, as well as the pharmaceutically, dietetically or cosmetically acceptable derivatives thereof, possess the same activity of reduction of free-radicals as tioctic acid.

It has been now surprisingly found that association of tioctic acid and cysteine and/or a pharmaceutically, dietetically or cosmetically acceptable derivative thereof, is particularly advantageous for the prevention and treatment of a

condition caused by oxidative stresses.

In the present invention, the expression "oxidative stress" means any physiological and/or pathological condition characterised by an increase of the production of peroxides and free-radicals in general, for example in conditions of physical or mental stress, protracted fatigue, acute viral disease, hepatic insufficiency, dysmetabolism, especially referred to diabetes, inflammatory processes, both acute and chronic, such as, for instance, asthma, rheumatic and rheumatoid arthritis, Crohn's disease and ulcerative colitis, which always bring about a free-radical damage beyond the levels useful for defensive purposes and involving also the interested tissues, and ageing as a consequence also of oxidative phenomena, etc.

The association acts also specifically for optimising the lipidic and carbohydrate metabolisms and reducing the intra- and extra-mitochondrial oxidative metabolism, which is the main source of free-radicals.

An aspect of the invention is a composition containing tioctic acid and cysteine and/or a pharmaceutically, dietetically or cosmetically acceptable derivative thereof, the concentration of each component amounting from 0,1 to 40,0% by weight, preferably between 0,1 and 20,0% by weight, and a pharmaceutically, dietetically or cosmetically, acceptable vehicle and/or excipient.

Among the pharmaceutically, dietetically or cosmetically acceptable derivative of cysteine, preferred are N-acetylcysteine, cystine and carboxymethyl cysteine, although any derivative could be selected by the skilled in the art.

A clear synergic effect deriving from the

combination of the above-mentioned molecules has been in fact observed and it can be supposed that an increase of the activity of the individual components of the composition of the invention on glutathione peroxidase is the cause of such a surprising result. A further synergic effect improves the efficiency of mitochondrial oxidative metabolism, consequently reducing the free-radicals.

It has now been found that the compositions of the invention are useful for preparing a drug, a cosmetic or a dietetic supplement for the prevention and/or treatment of physiological and/or pathological conditions caused by oxidative stresses involving, therefore, an increase of production of free-radicals (peroxides, etc.)

The composition of the invention is therefore useful for the prevention and/or treatment of physical and/or mental stress, pain and asthenia, the Down's syndrome, chronic degenerative pathologies, such as Alzheimer's disease, acute and chronic viral diseases, hepatic insufficiency, dysmetabolism, particularly in the clinical conditions of decreased tolerance to glucose characterised by hyperinsulinism and weight increase, diabetes, obesity, membranopathies as liposclerosis and cellulitis; cardiopathies, particularly those characterised by vasospasms, for example angina pectoris, myocardium infarction, for the protection of coronary vessels, prevention and/or treatment of ischemia.

The compositions of the invention are further useful for the prevention and/or treatment of viral pathologies, particularly herpes, influenza and B and C hepatitis.

It has been observed a clear improvement of patients affected by immunopathologies, particularly the ones involving immunoregulation and the acquired immuno-deficiency syndrome (AIDS).

The composition of the invention proved to be surprisingly useful in the treatment of climacteric and pre-menstrual syndromes and during pregnancy which is a physiological state accompanied by a high metabolic rate and consequently elevated production of reactive oxygen species (ROS). Particularly, pre-eclampsia, a pregnancy-specific condition characterised by hypertension and proteinuria both of which remit after delivery, is associated with increased lipid peroxidation in the maternal circulation and in placenta compared with the ones measured during normal pregnancy. Even the humour tone (depression), which is a side, but very frequent, symptom of menopause and after delivery, has been improved by the administration of the compositions of the invention, which show clearly their usefulness also in the treatment of depression or anxiety conditions.

Further, the composition of the invention showed to be useful for the preparation of a medicament for the prevention and the treatment of sperm motility: the production of sperm-generated ROS is accelerated in defective sperm and it highly correlates with impairment in sperm motility. The ability of the composition of the invention to hinder the formation of free radicals resulted to be useful also for increasing the fertilisation rate in asthenospermic people.

Still further, the compositions of the invention proved to be useful for the prevention and/or the treatment of malignant and benign tumors,

particularly of cheloids.

Also the prevention and/or the treatment of retinitis pigmentosa, cataract and age related macular degeneration proved to be possible using the compositions of the invention.

It has been still further observed an increased fatigue resistance, a protein saving power and a protection of muscles under stress from the oxidative damages.

From the experimental data of tests carried out on athletes, a significant decrease of fat mass has been observed, even in anaerobiosis conditions. The lipid reduction is higher in the sites where the lipid content is higher, which suggests an optimal normalisation of oxidative metabolism of lipids.

The anti-free-radicals activity of the compositions of the invention makes them suitable also for the preparation of topical, pharmaceutic and cosmetic formulations (creams, ointments, salves, etc.) and of a dietetic supplement for preventing and treating general atopy, atopical dermatitis, psoriasis, acne, bedsores, solar erythemas, and for hindering the process of ageing, particularly skin ageing, hair loss, the damages induced by smoke and for the protection of muscles stress from oxidative damages.

The compositions of the invention are also useful for the preparation of a drug for the prevention and treatment of phlebopathies, such as ulcers, and inflammatory phenomena, conditions wherein the presence of free-radicals is usually high, an analgesic effect being also observed.

The surprising synergic effect shown by the association of tioctic acid and cysteine and/or a pharmaceutically, dietetically or cosmetically

acceptable derivative thereof can be further increased by addition to the compositions of the invention of other anti-free-radical agents, such as coenzyme Q10, folic acid, carnitine (or a carnitine derivative which can be easily selected by the skilled in the art, such as the methyl-, propyl- carnitine, etc.), vitamins B, C and E, flavonoids, pantothenic acid, terpenes, tannins, natural extracts such as Tarchonanthus Canphoratus L (both as an essential oil and as an extract), oligo-elements, for example selenium, chromium, zinc, copper etc., polyphenols, resveratrol, anthocyanidins, or essential fatty acids, for example the omega-3-ones (for example, by employing oils with a high content of such acid, such as linseed oil, perilla oil, etc.), phytoestrogens (for example those extracted from soybeans) and aminoacids (glutamine, glutamic and aspartic acids, etc.), each one in amounts between 2 and 8% by weight.

The compositions of the invention can further comprise, preferably, melatonine, alone or conjugated with adenosine, or one of its derivatives, such as 2-bromomelatonine, and/or allantoine, each one in amounts of 0.5-5.0% by weight.

It is also preferable adding to the compositions of the invention a medium-chain (C_6-C_{12}) triglyceride, in amounts of 5-40% by weight.

The compositions of the invention can be obviously formulated, depending on the selected realisation form, administration route and specific purposes, by employing the usual pharmaceutic, dietetic and cosmetic techniques known by those skilled in the field.

The compositions of the invention can be provided in the most different forms, according to their use and administration route, the subject to be treated, concentration etc., on the basis of the knowledge of those skilled in the field. Particularly preferred are tablets and capsules, but also powders, granules to be dispersed in water, pills, even the effervescent ones, syrups, confectioneries, topical and injectable preparations, plasters for transdermal release, suppositories or solutions, emulsions and/or dispersions for aerosol.

Also the vehicles and/or excipients comprised in the compositions of the invention can be selected, according to the use, administration form etc., by those skilled in the field on the basis of their general knowledge.

For example, vehicles for the compositions of the invention can be liposomes, nanospheres, acrylic foams, cyclodextrins, etc., excipients can be magnesium hydroxide, magnesium oxide, vegetable extracts (such as, for example, soybean flour, wheat flour, wheat and soybean proteins, etc.), polysaccharides (such as, for example, cellulose, starches, etc.), polyalcohols (such as, for example, glycerol, sorbitol, mannitol, polyethylene glycol, etc.), lipids (such as, for example, sunflower oil, olive oil, karitè butter, alkyl esters of polyacids, alkyl maleate, alkyl tartrate), emulsifiers (such as, for example, ethoxylate alcohols, soaps, acyl glutamates), polymers as viscosity improving agents (such as, for example, acrylic resins, modified cellulose, guar gum, etc.), preservatives (such as, for example, imidazolidinylurea, phénoxyethanol,

parahydroxybenzoates, metallic silver, etc.), fragrances (such as, for example, compositions of essential, natural and synthetic, oils), coloring agents or pigments (such as, for example, carmine blue, tartrazine, titanium dioxide, zinc oxide, etc.), sweeteners (such as, for example, saccarose, sorbitol, aspartame, etc.).

Illustrative examples of the compositions of the invention, for specific applications and some preferred administration forms, are reported below.

1)Muscles under stress

Composition I for oral administration
(Preparation form: tablets, capsules, etc.)

	mg/dose
Tioctic acid	50-200
Cysteine*	50-200
Magnesium hydroxide	100-200
Vitamin B1	0.5-1.5
Vitamin B2	0.5-2
Vitamin B3	10-50
Glutamine	20-100
Nicotinic acid	5-30
Pantothenic acid	10-30
Phosphocreatine	0.1-0.5
Excipients, binders, flavoring agents, coloring agents, sweeteners etc.	q.s.

* or N-acetylcysteine, cystine and carboxymethyl cysteine

In sports the association with medium chain triglycerides (C_6-C_{12}), in doses of 5-40% by weight, is preferred.

Composition II for topical administration
(Preparation form: emulsion, cream, ointment, etc.)

	%
Tioctic acid	0.10-5.00
Cysteine*	0.10-5.00
Rosemary (extract produced by INDENA)	1-3
Tocopheryl nicotinate	0.10-1.00
Escin (produced by INDENA)	0.10-5.00
Centella asiatica (produced by INDENA)	0.10-5.00

Vitamin E	0.05-1.00
Glycirrhetic acid or derivatives (produced by NIKKO)	0.05-1.00
Hyaluronic acid	0.01-0.50
Polysaccharides	0.01-1.00
Polyalcohols	1.00-5.00
Lipids	10.0-40.0
Emulsifiers	2.00-5.00
Polymer viscosity improving agents	0.02-1.00
Derivatives, fragancies, coloring agents and pigments	q.s.

* or N-acetylcysteine, cystine and carboxymethyl cysteine

2) Cardiac pathologies

Composition III for oral administration
(Preparation form: tablets, capsules etc.)

	mg/dose
Tioctic acid	50-200
N-acetylcysteine*	50-200
Magnesium hydroxide	100-200
Linseed oil	200-400
Vitamin E	5-20
Vitamin C	30-200
Selenium methionine	10-50 µg
Coenzyme Q10	50-150
Acetyl carnitine	300-700

* or cysteine, cystine and carboxymethyl cysteine

3. Hyperinsulinism altered carbohydrate tolerance, diabetes and obesity

Composition IV for oral administration
(Preparation form: tables, capsules, etc.)

	mg/dose
Tioctic acid	50-200
Cysteine*	50-200
Magnesium hydroxide	100-200
Chromium picolinate	100-300 µg
Algae	100-400
Omega-3 fatty acids	200-400

* or N-acetylcysteine, cystine and carboxymethyl cysteine

4) Liposclerosis

Composition V for oral administration
(Preparation form: tables, capsules, etc.)

	mg/dose

Tioctic acid	50-200
Cysteine*	50-200
Glutamine	50-100
Magnesium Hydroxide	150-200
Vitamin B1	0.5-1.5
Vitamin B2	0.5-2
Vitamin B3	10-50
Guaranà (produced by Agrar)	50-100
Yombina (produced by Agrar)	1-10

* or N-acetylcysteine, cystine and carboxymethyl cysteine

The example of formulation of above can also comprise other active ingredients, in doses of 2-8% by weight, selected from: caffeine, guaranà, escin/horse-chestnut (produced by INDENA), ivy (produced INDENA), echinacea (produced by INDENA), gingko biloba (produced by INDENA), quercetin (produced by BRACCO).

Composition VI for topical administration

	%
Tioctic acid	0.1-5.0
Cysteine*	0.1-5.0
Guaranà (produced by Agrar)	0.5-1.0
Caffeine	0.1-0.5
Nicotin acid	0.005-0.050
Ginko biloba phytosoma (produced by Indena)	0.2-2.0
Borage oil (produced by P. GIANNI)	0.20-2.0
Tocopherol	0.05-0.5
Tocopheryl acetate	0.05-0.5
Glycirrhetic acid (derivatives) (produced by NIKKO)	0.02-0.5
Centella asiatica (produced by INDENA)	0.50-5.0
Sericoside phytosoma (produced by INDENA)	0.20-5.0
Ethil ximeninate (produced by INDENA)	0.10-2.00
Tocopheryl nicotinate	0.015-0.50
Hyaluronic acid (produced by A.ERRE)	0.015-0.50
Polysaccharides	0.01-0.5
Polyalcohols	0.01-1.0
Yombima (produced by Agrar)	1.00-5.0
Lipids	0.5-2
Emulsifiers	10-40
Polimer viscosity improving	2.0-5.0

agents)	
Preservatives, fragancies, coloring agents and pigments	0.02-1.0

* or N-acetylcysteine, cystine and carboxymethyl cysteine

5) Hepatic insufficiency

Composition VII for oral administration
(Preparation form: tablets, capsules, etc.)

	mg/dose
Tioctic acid	50-200
Cysteine*	50-200
Magnesium hydroxide	100-200
Cochlospernum t. extract (produced by INDENA)	50-200
Vitamin B1	0.5-1.5
Vitamin B2	0.5-2
Vitamin B3	10-50
Vitamin K	1-5
Selenium methionine	10-50 µg

* or N-acetylcysteine, cystine and carboxymethyl cysteine

6) Menopause/humour tone

Composition VIII for oral administration
(Preparation form: tablets, capsules, etc.)

	mg/dose
Tioctic acid	50-200
Cysteine*	50-200
Magnesium hydroxide	100-200
Sayabeen phystoestrogeus (produced by Agrar)	10-30
Vitamin B1	0.5-1
Vitamin B2	0.5-2
Vitamin B3	10-50
Vitamin E	2-20
Vitamin C	30-200

* or N-acetylcysteine, cystine and carboxymethyl cysteine

7)Viral pathologies

Composition IX for oral administration
(Preparation form: tablets, capsules, etc.)

	mg/dose
Tioctic acid	50-200
Cysteine*	50-200
Magnesium hydroxide	100-200
Vitamin E	5-20
Vitamin C	20-200
Zinc	20-60

Selenium methionine	10-50 µg
Echinacea (produced by INDENA)	100-300
Propolis (produced by AGRAR)	50-100

* or N-acetylcysteine, cystine and carboxymethyl cysteine

8) Dermatological pathologies

Composition X for oral administration
(Preparation form: tablets, capsules, etc.)

	mg/dose
Tioctic acid	50-200
Cysteine*	50-200
Magnesium hydroxide	100-2000
Vitamin E	5-20
Vitamin C	20-200
Betacarotene (produced by AGRAR)	2-10
Ozonized oil (produced by OZONOIL)	50-200

* or N-acetylcysteine, cystine and carboxymethyl cysteine

Composition XI for topical administration
(Preparation form: cream, ointment, ...)

	%
Tioctic acid	0.10-5.0
Cysteine*	0.10-5.0
Macadamia nut oil (produced by AGRAR)	0.50-5.0
Ceramide (produced by QUEST)	0.1-0.3
Tocopherol (produced by P.GIANNI)	0.05-0.5
Tocopheryl acetate (produced by P.GIANNI)	0.05-0.5
Glycirrhetic acid (produced by INDENA)	0.05-0.5
Hyaluronic acid (produced by A.ERRE)	0.01-0.5
Polysaccharides	0.10-1.0
Polyalcohols	1.00-5.0
Lipids	10-40
Emulsifiers	2.0-5.0
Polymer viscosity improving agents	0.02-1.0
Preservatives, fragrancies coloring agents, pigments	q.s

* or N-acetylcysteine, cystine and carboxymethyl cysteine

Composition XII for topical administration

(Preparation form: cream, ointment, etc.)

	%
Tioctic acid	0.10-5.0
Cysteine*	0.10-5.0
Mulberry extract (produced by CFM)	0.20-2.0
Soyabean proteins (produced by CASTELLI)	0.20-2.0
Borage oil (produced by AGRAR)	0.50-5.0
Macadamia nut oil (produced by AGRAR)	0.50-5.0
Ceramide (produced by QUEST)	0.20-2.0
Panthenol (produced by P.GIANNI)	0.40-4.0
Vitamin C (produced by P.GIANNI)	0.50-3.0
Tocopherol (produced by P.GIANNI)	0.05-0.5
Tocopheryl acetate (produced by P.GIANNI	0.05-0.5
Glycirrhetic acid (produced by INDENA)	0.05-0.50
Polysaccharides	0.10-1.0%
Polyalcohols	1.00-5.0%
Lipids	10-40
Emulsifiers	2.0-5.0
Polymer viscosity improving agents	0.02-1.0
Preservatives, fragrancies, coloring agents, pigments	q.s

* or N-acetylcysteine, cystine and carboxymethyl cysteine

9) Phlebopathies

Composition XIII for oral administration
(Preparation form: tablets, capsules, etc.)

	mg/dose
Tioctic acid	50-200
Cysteine*	50-200
Ginkgo biloba (produced by INDENA)	50-200
Escin	50-200
Vitamin E (produced by BRACCO)	5-20
Vitamin C (produced by BRACCO)	20-200
Acetyl salicilate (produced by CFM)	50-100
Pineapple extract (produced by AGRAR)	50-500

* or N-acetylcysteine, cystine and carboxymethyl cysteine

Composition XIV for oral administration

	mg/dose
Tioctic acid	50-200
Cysteine*	50-200
Flavonoids	50-200
Troxirutin (produced by BRACCO)	50-200
Vitamin B1	0.5-1.5
Vitamin B2	0.5-2
Vitamin B3	10-50

* or N-acetylcysteine, cystine and carboxymethyl cysteine

Composition XV for topical administration

	%
Tioctic acid	0.10-5.0
Cysteine*	0.10-5.0
Borage oil (produced by AGRAR)	0.50-5.0
Tocopherol (produced by P.GIANNI)	0.05-0.5
Tocopheryl acetate (produced by P.GIANNI)	0.05-0.5
Glycirrhetic acid (produced by INDENA)	0.05-0.5
Centella asiatica (produced by INDENA)	0.50-5.0
Sericoside (produced by INDENA)	0.50-5.0
Ethyl ximeninate (produced by INDENA)	0.20-5.0
Hyaluronic acid (produced by A-ERRE)	0.01-0.5
Polysaccharides	0.01-1.0
Polyalcohols	1.00-5.0
Lipids	10-40
Emulsifiers	2.0-5.0
Polymer viscosity improving agents	0.02-1.0
Preservatives, fragrancies, coloring agents, pigments	q.s.

* or N-acetylcysteine, cystine and carboxymethyl cysteine

Composition XVI for topical administration

	%
Tioctic acid	0.10-5.0
Cysteine*	0.10-5.0
Phytosterols	1.00-3.0
Borage oil (produced by AGRAR)	0.50-5.0
Tocopherol (produced by INDENA)	0.05-0.5
Tocopheryl acetate (produced by P.GIANNI)	0.05-0.5

Glycirrhetic acid (produced by INDENA)	0.05-0.5
Troxirutin (produced by BRACCO)	0.20-5.0
Escin (produced by INDENA)	0.20-2.0
Ginkgo biloba (produced by INDENA)	0.20-5.0
Comarin (produced by AGAR)	0.20-2.0
Arginine (produced by AJNOMOTO)	0.10-1.0
Polysaccharides	0.01-1.0
Polyalcohols	1.00-5.0
Lipids	10-40
Emulsifiers	2.0-5.0
Polymer viscosity improving agents	0.02-1.0
Preservatives, fragrancies, coloring agents, pigments	q.s.

* or N-acetylcysteine, cystine and carboxymethyl cysteine

10) Skin ageing

Composition XVII for oral administration (Preparation form: tablets, capsules, etc.)

	mg/dose
Lipoic acid	50-200
Cysteine*	50-200
Magnesium hydroxide	100-2000
Vitamin E	5-20
Vitamin C	30-200
Vitamin A	5.000-50.000 u
Jojoba ozonized oil (produced by OZONOZIL)	50-300
Selenium methionine (produced by MICRO)	10-50

* or N-acetylcysteine, cystine and carboxymethyl cysteine

Composition XVIII for topical administration (Preparation form: cream, emulsion, etc.)

	%
Tioctic acid	0.10-5.0
Cysteine*	0.10-5.0
Monomethylsilanol + mannuronic acid (produced by EXIMOL)	0.20-3.0
Methylsilanol spirulinate	0.30-3.0
Algae extract	0.30-3.0
Hydrolysed soyabean flour	0.30-3.0
Leucocyanidrine	0.20-2.0
Macadamia nut oil	0.50-5.0
Ceramide	0.20-2.0
Tocopherol	0.05-0.5
Tocopheryl acetate	0.05-0.5
Glycirrhetic acid	0.05-0.50

Polysaccharides	0.10-1.0
Polyalcohols	1.00-5.0
Lipids	10-40
Emulsifiers	2.00-5.0
Polymer viscosity improving agents	0.02-1.0
Preservatives, fragrancies, coloring agents, pigments	q.s

* or N-acetylcysteine, cystine and carboxymethyl cysteine

Composition XIX for topical administration (containing all the ingredients of the above composition and the following α-hydroxyacids)

	%
Citric acid	0.50-2.0
Malic acid	0.50-2.0
Tartaric acid	0.50-2.0
Lactic acid	0.50-2.0
Glycolic acid	0.50-2.0

or analogous keto-acids (such as for example pyruvic acid).

The example of any of the above compositions can also provide the association with melatonine in doses of 0.5-5.0% by weight (alone or conjugated with adenosine, or its derivatives, for example 2-bromomelatonine) or, as far as compositions XI and XII are concerned, also with allantoine, in doses of 0.50-5.0% by weight.

The following examples illustrate the invention without limiting it.

EXAMPLE 1

Muscles under stress

N-acetylcysteine (200 mg) and magnesium hydroxide (150 mg) are mixed and powdered in a mortar and then tioctic acid (200 mg) is added until an homogeneous mixture is obtained. With the above obtained mixture, type O gelatine capsules (produced by CAPSUGEL PARK DAVIS) are filled.

The preferred composition was orally administered

[tioctic acid (10 mg/Kg/day) and N-acetylcysteine (10 mg/Kg/day)] to twelve athletes of body building, for a period of 45 or 60 days, and weight and fat percent were controlled by plicometry.

The values of athletes with 60 days of treatment show a decrease of weight (4%) and a sharp decrease of fat percentage (7%). There is an improvement of proteic mass of the muscle of 3%.

As far as data of the group whose treatment was interrupted after 45 days are concerned, a decreasing trend, even if less sharp, is observed also after the interruption.

Athletes with supplement for 60 days

ATHLETES	AGE 28-44	INITIAL WEIGHT KG	INITIAL FAT %	45 DAYS FAT %	60 DAYS WEIGHT KG	60 DAYS FAT %
1)MA	34	84.8	12.6	6	81.1	4.1
3)CR	34	82.9	9.4	5.4	80.2	4.0
4)GF	32	88.5	10.6	6.3	86.5	3.6
5)BR	44	94.7	9.5	6.1	92.5	3.5
8)RR	29	86.7	14.1	7.8	84.0	4.9
9)RM	40	114.5	14.4	7.5	103.3	4.8
11)MG	38	102.4	10.6	6.7	100.4	4.9
12)RA	40	98.6	8.9	5.6	97.0	3.4
AVERAGE	36.4	94.1	11.3	6.4	90.6	4.2
SIGMA	5.0	10.7	2.2	0.9	8.9	0.6
Prob=66%						
Lower Threshold		83.4	9.1	5.6	81.7	3.5
Higher Threshold		104.9	13.4	7.3	99.6	4.8
Width		21.4	4.3	1.7	17.9	1.3

Athletes with supplement for 45 days

ATHLETES	AGE 28-44	INITIAL WEIGHT KG	INITIAL FAT %	45 DAYS FAT %	60 DAYS WEIGHT KG	60 DAYS FAT %
2) LL	28	86.4	14.3	6.5	81.3	5.5
6) SG	31	79.4	10.8	6.4	74.3	5.2
7) RC	33	88.5	11.4	6.3	81.2	5.7
10) PM	31	96.8	14.8	6.8	88.3	5.7
AVERAGE	30.8	87.8	12.8	6.5	81.3	5.5
SIGMA	2.1	7.2	2.0	0.2	5.7	0.2
Prob=66%						
Lower Threshold		80.6	10.8	6.3	75.6	5.3
Higher Threshold		94.9	14.8	6.7	87.0	5.8
Width		14.3	4.0	0.4	11.4	0.5

The statistical analysis of data shows that the percent reduction of fat tends to a lower dispersion (standard deviation or width). The composition of the invention seems therefore tending to regulate the fat percent in the muscles to a constant value.

The fat reduction effect is more evident clear where the percentage is more shifted from the ideal physiologic value. All the athletes pointed out a minor fatigue and a better resistance during the training.

EXAMPLE 2

Hepatic insufficiency

The composition of Example 1 was orally administered [tioctic acid (10 mg/Kg/day) and N-acetylcysteine 10 mg/kg/day)] to twelve patients and the hepatic functionality was then evaluated.

A) values determined before the administration of the composition of the invention.

B) values determined 45 days after the

administration (3 patients spontaneously interrupted the administration of the composition)

GPT = glutamic - pyruvic transaminase

GOT = glutamic - oxalacetic transaminase

TG = triglycerides

Patient	MA		LL		CR		GF	
	A	B	A	B	A	B	A	B
GPT	60	23	96	40	78	41	41	31
GOT	42	18	65	22	53	34	36	18
TG	260	192	190	135	280	147	150	102

Patient	BR		SG		RC		RR	
	A	B	A	B	A	B	A	B
GPT	115	54	56	41	91	-	32	28
GOT	92	91	52	28	75		22	20
TG	361	163	214	115	272		169	116

Patient	RM		PM		MG		RA	
	A	B	A	B	A	B	A	B
GPT	124	41	42	-	102	64	88	-
GOT	92	28	38	-	84	41	91	-
TG	301	110	154		209	131	284	-

The table below reports the values of the transaminases measured before and 45 days after the administration of the composition.

PATIENT	GPT	GPT45	GOT	GOT45	TG	TG45
MA	60	23	42	18	260	192
II	96	40	65	22	190	135
CR	78	41	53	34	280	147
GF	41	31	36	18	150	102
BR	115	94	92	91	361	163
SG	56	41	52	28	214	115
RR	32	28	22	20	169	116
RM	124	41	92	28	301	110

MG	102	64	84	41	209	131
AVERAGES	78.2	44.7	59.7	33.3	237.1	134.6
SIGMA	32.9	21.8	25.3	22.9	68.5	28.9

The data analysis allows a clear improvement of hepatic metabolism to be observed.

The reduction of the free-radicals obtained by the administration of the composition of the invention has therefore brought about a hepatoprotective activity with the reduction of transaminases. The reduction of the triglycerides is supposed to be dependent on a better mitrochondrial utilisation.

EXAMPLE 3

Menopause/humour tone

The composition of Example 1 [tioctic acid (200 mg/Kg/day) and N-acetylcysteine (200 mg/Kg/day)] was orally administered to five women 42-51 years old, for three months.

Further, the psychological conditions of the five women were evaluated according to the Hamilton method by determining the levels of the luteo-plasmatic hormone and the "social satisfaction"

Luteo-plasmatic hormone (U.I./g)

SUBJECTS	INITIAL	AFTER 3 MONTHS
PL	61	51
VT	49	45
DT	50	44
FS	29	41
CE	75	50
AVERAGE	52.8	46.2
SD	18.84	3.74

HAMILTON TEST

Depression scale according to Hamilton

EUPHORIA	< 30
NORMAL CONDITION	30-35
DEPRESSION	> 35

SUBJECTS	INITIAL	AFTER 3 MONTHS
PL	56	36

VT	56	41
DT	43	31
FS	51	36
CE	49	34
AVERAGE	51	35.6
SD	5.38	4.20

"Social satisfaction": self-evaluation scale to social adaptation - Normal values: 35-52

PL	27	39
VT	31	41
DT	25	46
FS	20	35
CE	32	38
AVERAGE	27	40
SD	5.60	4.69

All the subjects who received the treatment showed a sharp improvement of the humour and even more of the "social satisfaction".

The administration of the composition of the invention has brought about a sharp improvement for the subjects in menopause.

The reduction of the luteo hormone further shows a decrease of fatty tissues.

EXAMPLE 4

Viral pathologies

The number of infections and their seriousness were evaluated in six healthy children between 4 and 6 years old by oral administration of the composition obtained by mixing and powdering in a mortar: N-acetylcysteine (50 mg) and magnesium hydroxide (30 mg) were admixed then adding tioctic acid (50 mg) until an homogeneous mixture was obtained. With this mixture, gelatine capsules type O (produced by Capsugel Park Davis) were filled. An analogous, but non-treated, group of children, was utilised as control.

The evaluation, for more than three months, was carried out when all the children, even those of

the control group, attended the nursery school.

The number of infectious events of viral nature, treated with symptomatic drugs, their average duration and the arising of complications (otitis, sinusitis, tonsillitis, bronchitis, for which the antibiotic therapy was necessary), were determined.

	age	N. of infective events	average duration	complications
AL	3	3	3 days	2
CM	4	2	2.5	1
BE	4.5	1	3	0
MM	4.5	2	2	0
BA	5	1	2	0
BE	6	1	2	0

Control group

	Age	N. of infective events	average duration	complications
IC	3	4	5 days	2
BM	4	3	5	2
FF	4.5	3	4	1
AS	4.5	3	4	1
CA	5	2	3	0
BL	6	2	3	0

The effectiveness of the composition of the invention for reducing the number of infections events and their seriousness has been therefore proved.

EXAMPLE 5

Dermatological pathologies

Six psoriasis patients were treated with the following emulsion "E1" daily applied and prepared as follows:

PHASE A	%
Tioctic acid (produced by Antibioticos)	0.5
N-acetylcysteine (produced by Agar)	0.5

Ethanol alcohol (produced by Orbat)	10
Ceramide (produced by Quest)	0.2
Lecithin (produced by Rhone Poulenc)	2.5
Deionized water	20
PHASE B	
Deionized water	a 100
Dipotassium glycirrhate (produced by Nikkon)	0.005
Fucogel (polysaccharides by CFM)	3
Glycerol (produced by Henkel)	1.5
1.3-butylen glycol (produced by LCM)	1.5
Imidazolidinyl urea	0.25
Phenoxy ethanol	0.25
Carbopol 2000 (produced by Biochim)	0.2
Pemulen TR-2 (produced by Biochim)	0.5
PHASE C	
Alkyl maleate (produced by Condea)	2
Alkyl tartrate (produced by Condea)	2
Macadamia nut oil (produced by Balestrini)	1
Shorea butter (produced by Gianni)	1
Jojoba oil (produced by Balestrini)	1
PHASE D	
Triethanolamine (produced by Gianni)	0.7
PHASE E	
Fragrancies(CONC 40648 produced by CERIZA)	0.2

Phase A: a dispersion of ethanol in lecithin and in the other components is preferred, water is then added and the mixture is emulsified for 10 minutes.

Phase B: in a dispersion of Carbopol 2000 and Pemulen TR-Z in water at 70°C the other components are dissolved.

Phase C: the components are mixed by heating to 70°C and the phase C is dispersed into the phase B by emulsifying for 10 minutes; phase D is added by

uniformly mixing and the mixture is cooled. At 40°C the phase A is added by continuously cooling under uniform mixing, the phase E is then added. Cooling is continued till 30°C.

With the same procedure of emulsion "E1", also the emulsion "E2", containing tioctic acid and N-acetylcysteine, both in amounts of 1,25% by weight, and emulsion "E3", containing tioctic acid and N-acetylcysteine, both in amounts of 2,5% by weight, were prepared.

In order to test more clearly the emulsions of the invention, the test was carried out in winter when psoriasis worsens.

Effects on the skin

Patient	Age	m/f	Treatment	Seriousness/Site	Results
MM	42	m	E1 for 15 days	+knee	regression
CF	23	m	E1 for 30 days	+elbow	regression
BML	51	f	E2 for 30 days	+++plantar	excellent
CA	30	m	E3 for 15 days	+elbow	good
VP	35	m	E3 for 20 days	++limbs	good
CC	75	m	E3 for 20 days	++limbs/knee	fair

EXAMPLE 6

Phlebopathies

The composition of Example 1 [tioctic acid (200 mg/day) and N-acetyl cysteine (200 mg/day)] was added to the usual anti-coagulative therapy based on coumarin derivatives and administered to 4 women 50 and 65 years old, respectively, suffering from deep thrombophlebitis of the lower limbs, for 2 months. The signs of the venous stasis, clinically assessed by congestion, cyanosis and edema, showed a faster regression in comparison with other patients of the same pathology and in analogous

conditions, treated with the coumarin-derivatives alone. The patients complained lower pain and discomfort and had less resort to anti-inflammatory and/or analgesic drugs.

The above composition of the invention was also administered to six patients, affected by chronic venous insufficiency, for 3 months but with a double daily dose [tioctic acid (400 mg/day) and N-acetylcysteine (400 mg/day)]. A sharp regression of some symptoms, such as, for example, heaviness of the legs, tingling and evening oedema, was observed just after 15 days of therapy.

For the evaluation of the results the following quantitative scale has been employed:

0	no reduction
1	moderate reduction
2	middle reduction (>30%)
3	excellent reduction (>50%)
4	complete disappearance

PATIENT	AGE	LEG HEAVINESS	TINGLING	OEDEMA
AL	45	2	3	2
BM	51	2	2	2
DR	48	3	3	2
CD	54	2	2	1
BL	47	1	1	0
MM	56	2	2	1

EXAMPLE 7

CLINICAL TEST ON VOLUNTEERS AFFECTED BY LIPOSCLEROSIS

A cream of the invention (composition VI), containing 2% tioctic acid / 2% cysteine was compared with a cream containing a placebo formula, using a double blind test.

A standard population of women 22-40 years old affected by liposclerosis (cellulitis) was separated in two groups in a random way. The

parameters to be evaluated during the test were not significantly different as controlled using the Student's t test.

1) GS Study Group: 15 women applied the cream of the invention
2) GC Control Group: 16 women applied the placebo cream

All the volunteers applied the creams daily for a month and were submitted to physical standardized activity (watergym) for two hours a week in two sections.

The diet was free and it was controlled that the volunteers did not start any hormone therapy like oestrogen or slimming diet or important variation in the nourishment. The plicae on the thigh (QU = quadriceps plica, PT = kneecap plica, FE = femoral plica) and two circumferences (CR = root of thigh, CM = median thigh) were measured.

A statistical analysis of the results using the Student's t test was performed. The data did not show any difference between the two groups GS and GC before treatment. The measures regarding the thickness of plicae resulted lower in both groups, but only the data relating to group GS resulted to be statistically significative ($p < 0,005$).

The Student's t test was also performed between the two groups GS/GC as far as the percentual weight loss was concerned. The results were evaluated measuring the values of the plicae before (t0) and after (t1) the treatment, according to the following formula:

[(plica t0 - plica t1)/plica t0]x100

The results obtained, showed again to be statistically significative (QU = $p<0.005$, PT = $p<0.05$, FE = $p=0.05$) for each plica.

No significative decrease of the circumferences was noted after the treatment also because all volunteers were under controlled physical activity that have increased their muscular mass as already demonstrated on the body building test.

It is therefore possible to note that the cream of the invention reduces the subcutaneous fat and liposclerosis. The skin after treatment resulted smoother insofar as both appearance and touch are concerned; less nodules were noted too.

CONTROL GROUP (GC)

Code	QUO	QU1	PTO	PT1	FE0	FE1	CR0	CR1	CM0	CM1
FS.01	30,0	31,0	13,8	13,8	21,0	21,0	60,0	60,0	53,0	53,5
FS.02	31,4	30,4	20,0	19,0	12,2	12,1	59,0	58,5	54,0	53,0
FS.03	21,0	19,8	6,8	4,6	9,4	9,4	54,5	54,5	51,0	51,0
FS.04	24,2	23,2	12,2	12,0	32,0	30,0	60,0	60,0	53,0	53,0
FS.05	23,0	22,0	12,2	12,2	19,0	18,6	53,5	53,8	47,3	49,0
FS.06	26,0	25,8	16,2	16,2	33,0	32,0	63,0	62,5	57,5	55,0
FS.07	13,2	13,2	11,2	11,2	10,4	10,5	52,6	52,6	47,3	47,2
FS.08	37,2	37,2	26,0	26,0	21,8	22,0	57,0	57,0	50,5	51,0
FS.09	19,0	18,6	16,4	15,8	14,2	14,0	59,0	58,8	54,5	54,2
FS.10	12,0	12,0	9,0	8,6	16,2	15,5	52,0	51,8	49,6	48,8
FS.11	39,0	39,0	23,6	24,0	24,0	63,4	63,4	57,5	57,5	57,5
FS.12	23,2	22,6	16,4	16,0	28,6	28,2	55,0	54,5	49,2	49,8
FS.13	29,4	28,8	19,2	18,5	26,0	24,8	57,0	56,0	52,4	51,5
FS.14	15,0	14,2	7,0	6,8	6,2	5,8	54,5	54,0	50,0	49,4
FS.15	17,3	17,3	12,2	12,0	18,4	18,0	57,5	57,0	52,5	52,0
FS.16	33,2	32,8	17,8	17,2	17,6	17,0	56,6	56,0	52,8	52,2

STUDY GROUP (GS)

Code	QUO	QU1	PT0	PT1	FE0	FE1	CR0	CR1	CM0	CM1
FS.01	31,6	29,4	17,8	1,8	23,4	19,6	60,5	59,0	52,8	51,4
FS.02	27,0	27,4	13,6	13,2	23,0	23,3	58,0	58,0	49,5	49,5
FS.03	29,4	26,4	19,0	16,0	19,0	18,4	61,7	59,4	52,2	53,0
FS.04	21,4	20,0	11,0	9,0	9,9	9,4	56,6	56,8	49,4	49,4
FS.05	32,0	28,4	14,2	13,0	21,2	18,5	58,0	58,0	52,0	51,5
FS.06	20,0	20,0	18,5	15,3	15,0	15,0	55,5	55,5	54,0	54,0
FS.07	17,6	16,8	11,0	8,6	14,0	12,4	52,5	52,0	46,0	48,0
FS.08	16,6	14,4	16,6	13,5	19,0	14,5	52,7	53,0	49,8	46,0
FS.09	23,2	21,8	6,0	4,8	11,0	8,0	53,6	53,0	49,4	48,7
FS.10	9,2	8,5	9,5	8,6	8,2	7,0	51,8	51,0	47,0	47,5
FS.11	48,8	40,2	28,4	22,6	40,0	35,0	71,6	66,5	61,0	57,5
FS.12	15,6	15,0	11,8	11,0	11,0	10,2	53,0	52,4	47,8	47,4
FS.13	41,8	38,0	31,0	27,2	35,0	31,5	66,0	60,0	62,0	56,0
FS.14	23,0	20,1	14,4	12,8	18,4	15,5	53,0	51,0	46,7	47,0
FS.15	40,0	32,0	25,0	20,2	36,0	30,2	65,0	61,0	56,5	56,0

EXAMPLE 8

CHELOIDAL FIBROBLASTS

Cheloidal fibroblasts are neoformations of benign tumours isolated from cutaneous biopsies in burned patients. The composition of the invention proved to be suitable to inhibit the growth of the neoplastic cells.

Cheloidal fibroblasts were compared to normal dermis fibroblast to find out how the composition of the invention affected growth rate, using

hydrocortisone, a well known inhibitor of cellular proliferation, as a reference.

The behaviour of the single components of the composition of the invention [in the present case, water (100 g) and triethanolamine (2 g) were admixed, under heating, with tioctic acid (1 g) and cysteine (1 g)] was also studied and compared with the results obtained by using the composition of the invention.

Both kinds of fibroblasts were put on Integrid dishes of 60 mm of diameter and grate of 2 mm and DMEM (Dulbecco's modified Eagle medium) with bovine foetal serum, ampicillin and sodium pyruvate and incubated at 37°C with 5% of CO_2. Every culture was made in double.

The substances employed were added to the medium after the cells had stuck to the dishes:

Hydrocortisone: 0.1M (= 0.036 mg dissolved into 1 ml of ethyl alcohol, then into 25 ml of medium). 0.01M (1 ml of 0.1 M + 9 ml of medium, brought to 25 ml using the medium).

Tioctic acid: 0.1 M (= 0.041 mg dissolved into 25 ml of medium). 0.01M (1 ml of 0.1 M + 9 ml of medium, then into 25 ml of medium).

Cysteine: 0.1 M (=0,012 mg dissolved into 0.1M NaOH, then into 25 ml of medium). 0.01M (1 ml of 0,1 M + 9 ml of medium, then into 25 ml of medium).

Cultures were observed at the optical microscope and photographs were taken to control growth and to identify any morphological alteration of fibroblasts.

The behaviour and growth of the cells were observed for 10 days after the seeding. The fibroblasts were observed at the optical microscope and photographed

after 24 hours from the contact with the molecules under test.

1 CONTROL (medium not added with any substance):

a)normal fibroblasts showed a regular growth in the control medium. The growth reached the confluence after 72 h of incubation at 37°C (incubator with 5% of CO_2).

b) The same behaviour was reported for cheloidal fibroblasts. Both cellular lines showed a peculiar spindled morphology, normal size and no apparent suffering.

2)Wih HYDROCORTISONE O,01M in the medium

a)Normal fibroblast did not present any growth modification;

b)adversely, the growth of cheloidal fibroblasts, treated in the same way, clearly reduced: after 3 days there was no cell confluence and the culture looked like it was on the first day. After 9 days the number of cells had no increase compared to the first day culture but the morphology seemed to be altered with a reduced cytoplasm which shows granulation.

3)With cysteine 0,01M in the medium.

a)The effect of cysteine upon normal fibroblast was to slightly reduce growth.

b) Upon cheloids fibroblast the effect on growth rate seemed to be stronger with a marked inhibited growth all over the observation period. No morphological difference between cheloidal cells treated with cysteine and untreated cheloidal cells (control cells) was observed. Yet the cells treated with cysteine did not show any suffering adversely to the ones treated with hydrocortisone.

4) With Tioctic acid in the medium

a) Normal fibroblasts treated with tioctic acid at a constant concentration of 0,01M, did not show any growth modification;

b) cheloidal cells, treated in the same way showed morphological modification and no growth; the cell shape became starred with dark granulation at the end of the dendrites.

5) With Tioctic Acid (0,005M) + L-cysteine (0,005M):

a) normal fibroblasts grew rapidly with no apparent morphological modifications;

b) the cheloidal fibroblasts growth resulted to have been inhibited more when treated with both substances than when treated only with one of them; this binary treatment had also effects on cell suffering which became evident because of morphological modifications

Conclusions:

Normal fibroblasts did not show any morphological modification and no break in growth in the presence of hydrocortisone, tioctic acid and cysteine. Only the cultures with cysteine had a decreasing growth effect.

Cheloidal fibroblasts growth were inhibited when cultivated in the presence of hydrocortisone, tioctic acid or cysteine. This effect was remarkably stronger when cheloidal fibroblasts were cultivated with the composition of the invention.

Hydrocortisone induces granulation which is a symptom of cellular suffering. The effect of cysteine alone is to inhibit growth without inducing morphological alterations. Tioctic acid inhibits growth and causes an evident cellular suffering. The composition of the invention determined not only a growth inhibition higher than

the inhibition reported when tioctic acid and cysteine were provided separately, but it also determined cellular suffering.

For cheloidal cells the inhibitory effect upon growth resulted higher when both substances are provided together than when they are provided separately, whereas for normal fibroblast culture the effect upon growth is not remarkable, this little effect being similar to the one reported when only cysteine was provided to the cell culture.

EXAMPLE 9

ANTI-AGEING

The effect of the composition of the previous example was studied on cultured amniocytes, which are aged and spoiled cells. Aiming to perform chromosome analyses of the foetus, the cells present in the amniotic fluid, sampled during the second trimester of pregnancy, were cultured in a medium in an incubator at 37°C in a 5% CO_2 atmosphere.

A great number of cells (amniocytes) is present in about 20 ml of amniotic fluid derived from different foetal tissues. Yet the most part of amniocytes is not viable because they are too aged and spoiled by the prolonged permanence in the amniotic fluid. Only a little number of amniocytes (10-40) is viable and able to adhere to the bottom of the Petri dishes wherein the culture medium was put; thus, a single living cell can duplicate and originate a colony. The time necessary to obtain a colony of about 500 cells is about 7-9 days.

On these grounds, an experiment was set up to test the effect of the composition of the invention on cultured amniocytes.

Ten different samples of about 20 ml of amniotic fluid were used. After centrifugation, for each sample, the cell pellet was divided into four equal parts and distributed into four Petri dishes (Amniodishes-Celbio). 2 ml of culture medium "AMNIOMED" (Celbio) were added into each Petri dish. Two Petri dishes were used as control, adding the composition of the invention (6 mcg/ml of tioctic acid and 14 mcg/ml of cysteine) to the other two dishes.

All the Petri dishes were put in an incubator at 37°C with 5% CO_2 till cellular colonies suitable for foetal caryotype diagnosis were developed. The cultures were checked every two days and finally stopped and analysed after the colonies reached the dimension of about 500 cells.

By comparison with the controls, the cultures containing the composition of the invention showed an increase (ranging from 30% to 50%) of the number of the grown colonies in all cases and reached the dimension of 500 cells at least one day before the controls.

The addition of the composition of the invention to the culture medium was shown to be able to increase the number of the cells adhering and forming colonies. The percentage shows the ability of the inventive composition to rescue old and spoiled amniocytes, so that the whole number of viable cells results considerably increased. Besides, the composition of the invention was able to modify the culture medium conditions increasing also the speed with which amniocytes divided themselves so that the colonies reached the number of 500 cells one day before the controls.

Clinical test

Ten volunteers, 3 men and 7 women, 75 to 87 years old, were supplemented with 200 mg/die of tioctic acid and 200 mg/die of cysteine (composition I was supplemented) for two months.

All volunteers were not affected by peculiar pathologies and were under normal therapies for elder people (pressure control and cardiovascular function).

None of the volunteers had important infectious pathologies during the first two months of their monitoring; only four had rinitis with normal course and without any complication.

All the volunteers had a net reduction of asthenia and they felt more active and less sleepy during the day. Even the pain symptoms to the joints were significantly reduced.

It resulted that the composition of the invention improves the general state of good health. Five volunteers declared of having been hungrier, that demonstrates the state of good health obtained. The familiars noted greater quickness, memory and interest for life. Seven volunteers on ten asked to continue the supplementation when the supplement was suspended because of the positive effects that they subjectively had.

EXAMPLE 10

Lotion to prevent hair loss and to increase hair growth

	% W/W
01-DENATURATED ALCOHOL	44.00
02-TIOCTIC ACID	2.50
03-CYSTEINE,	2.5
04-LECITHIN,	2.00
05-PERFUME,	0.20
06-TOCOPHERYL NICOTINATE,	0.10

07-TOCOPHERYL LINOLEATE 0.05
08-CYCLOMETHICONE, 0.05
09-WATER 45.65
10-SODIUM HYDROXIDE, 0.12
11-PEMULEN TR2 (Biochim) 0.20
12-SODIUM STEAROYLGLUTAMATE, 0.50

Solubilise in alcohol by stirring the above components 2, 3, 4, 5, 6, 7, 8 (A); solubilise sodium hydroxide in 10% of water (B); disperse in water at 60°C Pemulen TR2 (acrylates/C_{10}-C_{30} alkyl acrylate crosspolymer) (C), then add sodium stearoylglutamate.

Add B to C and cool until 30°C, then add (A) by stirring. Other two lotions were prepared replacing cysteine with cystine and carboxymethylcystine.

Ten volunteers, 25 to 40 years old, were invited to use the lotion two times a day for two months with a suitable massage.

All volunteers had a beginning of alopecia with a heavy daily hair loss. Five volunteers were also affected by seborrhoeic dermatitis.

After the treatment all volunteers were controlled recording the subjective results. All patients showed an improvement in the look of the hair which appeared energised, shining and easy to comb. The alopecia area did not increase as well as the thinning out.

The volunteers were invited to control the daily hair loss: in the morning they had to brush for 10 minutes and control the hair loss. They had to evaluate their loss according to the following scale:

1 very small loss, 2 small loss, 3 high loss, 4 very high loss.

During the first 15 days all volunteers had very high loss and at the end of the test reported that a reduced or very reduced number of hair could be found on their brushes. Also the seborrhoeic dermatitis resulted to be significantly reduced.

CLAIMS

1. A composition containing tioctic acid and cysteine and/or a pharmaceutically, dietetically or cosmetically acceptable derivative thereof, each one in an amount from 0,1 to 40,0% by weight, and a pharmaceutically, dietetically or cosmetically, acceptable vehicle and/or excipient.

2. A composition according to claim 1, wherein tioctic acid, cysteine and/or the pharmaceutically, dietetically or cosmetically acceptable derivative thereof amount, each one, from 0,1 to 20,0% by weight.

3. A composition according to claim 1 or 2, wherein the pharmaceutically, dietetically or cosmetically acceptable derivative of cysteine is selected from N-acetylcysteine, cystine and carboxymethyl cysteine.

4. A composition according to any one of the foregoing claims, containing at least one of the substances selected from the group of coenzyme Q10, folic acid, carnitine or a carnitine derivative, such as the methyl-, propyl- carnitine, vitamins B, C and E, flavonoids, pantothenic acid, terpenes, tannins, natural extracts such as Tarchonanthus Canphoratus L, both as an essential oil and as an extract, oligo-elements, such as selenium, chromium, zinc, copper, polyphenols, resveratrol, anthocyanidins, or essential fatty acids, such as the omega-3-ones, particularly linseed oil, perilla oil, phytoestrogens such as those extracted from soybeans and aminoacids such as glutamine, glutamic and aspartic acids, each one in amounts between 2 and 8% by weight.

5. A composition according to any of the foregoing claims, containing melatonine, alone or conjugated

with adenosine, one of its derivatives, such as 2-bromomelatonine, and/or allantoine, each one in amounts of 0,5-5,0% by weight.

6. A composition according to any of the foregoing claims, containing a medium-chain triglyceride (C_6-C_{12}) in amounts of 5-40% by weight.

7. Use of the composition according to any of the claims 1-6, for preparing a drug for the prevention and/or treatment of the physiological and/or pathological conditions deriving from oxidative stresses.

8. Use according to claim 7, for preparing a drug for the prevention and/or treatment of physical and/or mental stress.

9. Use according to claim 7, for preparing a drug for the prevention and/or treatment of pain and asthenia.

10. Use according to claim 7, for preparing a drug for the treatment of the Down's syndrome.

11. Use according to claim 7, for preparing a drug for the prevention and/or treatment of chronic degenerative pathologies, such as Alzheimer's disease.

12. Use according to claim 7, for preparing a drug for the prevention and/or treatment of viral diseases in acute and chronic phase.

13. Use according to claim 7, for preparing a drug for the prevention and/or treatment of immunopathologies.

14. Use according to claim 7, for preparing a drug for the prevention and/or treatment of hepatic insufficiency.

15. Use according to claim 7, for preparing a drug for the prevention and/or treatment of dysmetabolism.

16. Use according to claim 15, for preparing a drug for the prevention and/or treatment of clinical conditions of reduced tolerance to glucose, characterised by hyperinsulinism and/or weight increase.

17. Use according to claim 15 or 16, for preparing a drug for the prevention and/or treatment of diabetes.

18. Use according to claim 15 or 16, for preparing a drug for the prevention and/or treatment of obesity.

19. Use according to claim 15 or 16, for preparing a drug for the prevention and/or treatment of membranopathies, liposclerosis or cellulitis.

20. Use according to claim 7, for preparing a drug for the prevention and/or treatment of cardiopathies.

21. Use according to claim 20, for preparing a drug for the prevention and/or treatment of cardiopathies characterised by vasospasmus.

22. Use according to claim 20, for preparing a drug for the prevention and/or treatment of angina pectoris.

23. Use according to claim 20, for preparing a drug for the prevention and/or treatment of myocardium infarction.

24. Use according to claim 20, for preparing a drug for the protection of coronary vessels.

25. Use according to claim 20, for preparing a drug for the prevention and/or treatment of ischemia.

26. Use according to claim 7, for preparing a drug for the prevention and/or treatment of inflammatory phenomena.

27. Use according to claim 26, for preparing a drug for the prevention and/or the treatment of asthma,

rheumatic and rheumatoid arthritis, Crohn's disease and ulcerative colitis.

28. Use according to claim 26, for preparing a drug for the prevention and/or treatment of phlebopathies.

29. Use according to claim 7, for preparing a drug for the prevention and/or treatment of climacteric and/or pre-menstrual syndromes.

30. Use according to claim 7, for preparing a drug for the treatment of pre-eclampsia.

31. Use according to claim 7, for preparing a drug for the prevention and/or treatment of depressive forms and anxiety conditions.

32. Use according to claim 7, for preparing a drug for the prevention and/or the treatment of malignant and benign tumors.

33. Use according to claim 32, for preparing a drug for the prevention and/or the treatment of cheloids.

34. Use according to claim 7, for preparing a drug for the prevention and/or the treatment of retinitis pigmentosa, cataract and macular degeneration.

35. Use according to claim 7, for preparing a drug for the prevention and/or treatment of general atopy.

36. Use according to claim 35, for preparing a drug for the prevention and/or treatment of atopical dermatitis.

37. Use according to claim 7, for preparing a drug for the prevention and/or treatment of psoriasis.

38. Use according to claim 7, for preparing a drug for the prevention and/or treatment of acne.

39. Use according to claim 7, for preparing a drug for the prevention and/or treatment of bedsore.

40. Use according to claim 7, for preparing a drug for the prevention and/or treatment of viral pathologies.

41. Use according to claim 40, for preparing a drug for the prevention and/or treatment of influenza.

42. Use according to claim 40, for preparing a drug for the prevention and/or treatment of hepatitis and B and C, herpes virus and AIDS.

43. Use according to claim 7, for preparing a drug for the prevention and/or treatment of sperm infertility.

44. Use of the composition according to any of claims 1-6, for preparing a cosmetic for the prevention and/or treatment of physiological and/or pathological conditions deriving from oxidative stresses.

45. Use according to claim 44, for preparing an anti-ageing cosmetic.

46. Use according to claim 44, for preparing a cosmetic for the prevention and/or treatment of atopical dermatitis.

47. Use according to claim 46, for preparing a cosmetic for the prevention and/or treatment of psoriasis.

48. Use according to claim 44, for preparing a cosmetic for the prevention and/or treatment of erythemas.

49. Use according to claim 7, for preparing a cosmetic for the prevention and/or treatment of hair loss.

50. Use according to claim 44, for preparing a cosmetic for the protection of muscles stress from oxidative damages.

51. Use of the composition according to any of claims 1-6, for preparing a dietetic supplement for

the prevention and/or treatment of physiological and/or pathological conditions deriving from oxidative stresses.

52. Use according to claim 50, for preparing a dietetic supplement for the protection of muscles stress from oxidative damages.

53. Use according to claim 50, for preparing a dietetic supplement for the prevention and treatment of ageing.

INTERNATIONAL SEARCH REPORT

Inter nal Application No
PCT/EP 00/01637

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K31/385 //(A61K31/385,31:195)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 30228 A (NUTRI QUEST INC ;UNIV EMORY (US)) 16 July 1998 (1998-07-16) page 6, line 11 - line 27; claims 1-7 ---	1-4,12, 40,41
X	DE 43 28 871 A (BEIERSDORF AG) 2 March 1995 (1995-03-02) page 2, line 62 -page 3, column 15 tables ---	1-3,7, 36-39, 44-48,53
X	WO 98 33494 A (KOSBAB JOHN V) 6 August 1998 (1998-08-06) page 5, line 16 -page 6, line 26 page 10, line 19 - line 27 ---	1-5,17, 20

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
14 June 2000	20/06/2000
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Leherte, C

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INTERNATIONAL SEARCH REPORT

Inter nal Application No
PCT/EP 00/01637

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 292 538 A (ASHMEAD H DEWAYNE ET AL) 8 March 1994 (1994-03-08) column 2, line 27 - line 60 column 10 -column 12; examples claims	1-4
X,P	US 5 904 924 A (GAYNOR MITCHELL L ET AL) 18 May 1999 (1999-05-18) claims	1-4
A	US 4 990 330 A (OYAMA YASUAKI) 5 February 1991 (1991-02-05) abstract	1-53
A	FR 4 630 M (CENTRE D'ETUDES ET DE REALISATIONS THÉRAPEUTIQUES) 28 November 1966 (1966-11-28) page 2 -page 3	1-53

INTERNATIONAL SEARCH REPORT

International Application No. PCT/EP 00 01637

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1, 2, 4-53

Present claims 1, 2, 4-53 relate to an extremely large number of possible compositions and uses.
Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compositions claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compositions described in claim 3, with due regard to the examples of the description, and the general idea underlying the application.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter ›nal Application No
PCT/EP 00/01637

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